**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1. (Original) An isolated nucleic acid sequence of a mitotic checkpoint gene, *chfr*, which encodes a Chfr protein having a Forkhead-associated domain and a Ring Finger, wherein said protein is required for regulation of the transition of cells from prophase to metaphase.

2. (Original) The sequence according to claim 1, which is selected from the group consisting of:

(a) SEQ ID NO: 1 or an anti-sense sequence thereof,

(b) a sequence encoding at least amino acids 31 to 103 of SEQ ID NO: 2 or an anti-sense sequence thereof;

(c) a sequence encoding at least amino acids 303 to 346 of SEQ ID NO: 2 or an anti-sense sequence thereof;



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(d) a sequence encoding at least amino acids 476 to 641 of SEQ ID NO: 2 or an anti-sense sequence thereof;

(e) a sequence encoding at least amino acids 31 to 103, amino acids 303 to 346 and 476 to 641 of SEQ ID NO: 2 or an anti-sense sequence thereof; and

(f) a sequence having a homology of at least 50% to the sequences (a) through (e) according to a selected algorithm and encoding a protein or peptide having ubiquitin-protein ligase activity.

3. (Original) The sequence according to claim 1, which is synthetically or recombinantly produced.

4. (Original) The sequence according to claim 1, which is associated with a detectable label.

5. (Original) The sequence according to claim 1, which is present as a wild-type gene in normal human epidermal keratinocytes and normal human osteoblasts,

6. (Original) The sequence according to claim 1 that encodes a polypeptide that delays entry of a human cell into metaphase in response to mitotic stress.



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7. (Withdrawn) A substantially pure preparation of a polypeptide comprising a Forkhead-associated domain and a Ring Finger domain, wherein said protein is required for regulation of the transition of a normal human cell from prophase to metaphase.

8. (Withdrawn) The polypeptide according to claim 7, which is selected from the group consisting of

(a) SEQ ID NO: 2 or an complementary sequence thereof,

(b) a sequence comprising at least amino acids 31 to 103 of SEQ ID NO: 2 or an complementary sequence thereof;

(c) a sequence comprising at least amino acids 303 to 346 of SEQ ID NO: 2 or an complementary sequence thereof;

(d) a sequence comprising at least amino acids 476 to 641 of SEQ ID NO: 2 or an complementary sequence thereof;

(e) a sequence comprising at least amino acids 31 to 103, amino acids 303 to 346 and 476 to 641 of SEQ ID NO: 2 or an complementary sequence thereof; and



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(f) a sequence having a homology of at least 50% to the sequences (a) through (e) according to a selected algorithm and comprising a protein or peptide having ubiquitin-protein ligase activity.

9. (Withdrawn) The polypeptide according to claim 7, which is expressed in normal human epidermal keratinocytes and normal human osteoblasts.

10. (Withdrawn) The polypeptide according to claim 7 that delays entry of a human cell into metaphase in response to mitotic stress.

11. (Withdrawn) A method of determining tumorigenic potential of a cell comprising examining said cell for the presence of *chfr* nucleic acid sequence in said cell, wherein the absence of said *chfr* nucleic acid sequence indicates that said cell is predisposed to tumorigenesis upon exposure to mitotic stress.

12. (Withdrawn) The method according to claim 11, wherein said nucleic acid sequence is mRNA or genomic DNA.



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13. (Withdrawn) The method according to claim 11, wherein said examining step is selected from the group consisting of Northern blotting with a suitable nucleic acid probe, reverse-transcriptase PCR, RNase protection analysis and *in situ* hybridization.

14. (Withdrawn) A method of determining tumorigenic potential of a cell comprising examining said cell for the presence of Chfr polypeptide expression in said cell, wherein the absence of said polypeptide sequence indicates that said cell is predisposed to tumorigenesis upon exposure to mitotic stress.

15. (Withdrawn) The method according to claim 14, wherein said examining step is selected from the group consisting of Western immunoblotting, enzyme-linked immunoassay, immunofluorescence and immunohistochemistry.

16. (Withdrawn) A method for determining tumorigenic potential of a cell comprising examining said cell for mutations in the *chfr* gene, wherein the presence of mutations in said gene indicates that the cell is predisposed to tumorigenesis upon exposure to mitotic stress.



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17. (Withdrawn) The method according to claim 16, wherein said examining step comprises performing *in situ* hybridization.

18. (Withdrawn) The method according to claim 16, wherein said examining step comprises obtaining the nucleic acid sequence of the *chfr* gene in said cell and comparing said sequence to the sequence of a normal *chfr* gene to determine if the *chfr* gene of the cell bears a mutation.

19. (Withdrawn) The method according to claim 18, wherein said comparing step comprises performing conformation sensitive gel electrophoresis or single strand polymorphism analysis.

20. (Withdrawn) A method for determining tumorigenic potential of a cell comprising examining said cell for Chfr-mediated ubiquitin-protein ligase activity, wherein the absence of said activity indicates that the cell is predisposed to tumorigenesis upon exposure to mitotic stress.



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21. (Original) A diagnostic reagent comprising a nucleotide sequence that binds to the *chfr* nucleic acid sequence or a fragment thereof, said reagent sequence associated with a detectable label.

22. (Original) The reagent according to claim 21, which is an anti-sense fragment of SEQ ID NO: 1 or a fragment of said SEQ ID NO: 1.

23. (Original) A diagnostic reagent comprising a ligand which binds to Chfr, said ligand associated with a detectable label.

24. (Withdrawn) The reagent according to claim 23 wherein said ligand is selected from the group consisting of a polyclonal antibody, a monoclonal antibody or a recombinant antibody of classes IgG, IgM, IgA, IgD and IgE, a Fab, Fab' or F(ab')2, or Fc antibody fragment thereof which binds Chfr, a single chain Fv antibody fragment, a recombinant construct comprising a complementarity determining region of an antibody, a synthetic antibody or a chimeric antibody or a humanized antibody construct which shares sufficient CDRs to retain functionally equivalent binding characteristics of an antibody that binds said Chfr.



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25. (Original) A diagnostic kit for detecting the tumorigenic potential of a cell, said kit comprising a diagnostic reagent selected from the group consisting of a ligand which binds to Chfr, said ligand associated with a detectable label, and a nucleotide sequence that binds to the *chfr* nucleic acid sequence or a fragment thereof, said reagent sequence associated with a detectable label, and further comprising suitable components for detection of said label.

26. (Withdrawn) A diagnostic kit for detecting the tumorigenic potential of a cell comprising components for a chfr-mediated ubiquitin protein ligase assay.

27. (Original) A composition which inhibits the biological activity of Chfr.

28. (Withdrawn) The composition according to claim 27, which is a ligand which binds to Chfr and inhibits it biological activity.

29. (Withdrawn) The composition according to claim 28, wherein said ligand is selected from the group consisting of a polyclonal antibody, a monoclonal antibody or a recombinant antibody of classes IgG, IgM, IgA, IgD and IgE, a Fab, Fab' or F(ab')2, or Fc antibody fragment thereof which binds Chfr, a single chain Fv antibody



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fragment, a recombinant construct comprising a complementarity determining region of an antibody, a synthetic antibody or a chimeric antibody or humanized antibody construct which shares sufficient CDRs to retain functionally equivalent binding characteristics of an antibody that binds said Chfr.

30. (Withdrawn) The composition according to claim 27, which is a chemical compound.

31. (Withdrawn) A method of identifying a Chfr inhibitor, said method comprising the steps of:

(a) contacting a cell capable of expressing Chfr with a suitable amount of a test compound, and assessing the level of expression of Chfr in said cell;

(b) assessing the level of expression of Chfr in an otherwise identical cell which has not been contacted with said test compound; and

(c) comparing the levels of Chfr expression, wherein a lower level of expression of said Chfr in said cell (a) compared with the level of Chfr in said cell (b) indicates that said test compound is a Chfr inhibitor.

32. (Original) A Chfr inhibitor identified by the method of claim 31.



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33. (Withdrawn) A method of identifying a Chfr inhibitor, said method comprising the steps of:

screening a test compound in a Chfr-mediated ubiquitin-protein ligase assay, wherein the substantial absence of, or reduction in, said ligase activity in said assay in the presence of said test compound indicates that said test compound inhibits Chfr function.

34. (Withdrawn) The method according to claim 33 further comprising the step of contacting a mixture which normally demonstrates Chfr-mediated ubiquitin-protein ligase activity with a test compound; and assaying said mixture and test compound for said activity, wherein the absence of said activity in the presence of said test compound indicates that said test compound inhibits Chfr function.

35. (Withdrawn) The method according to claim 34, wherein said mixture comprises a labeled Chfr protein, the E1 ligase enzyme, the E2 ligase enzyme, ubiquitin and ATP.



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36. (Withdrawn) The method according to claim 34, wherein said assaying step comprises separating said labeled Chfr protein from said system, and performing gel electrophoresis thereon, and immunoblotting said gel with an anti-ubiquitin antibody, wherein the detection of ubiquitin in the gel by said antibody demonstrates Chfr-mediated ubiquitin-protein ligase activity.

37. (Withdrawn) The method according to claim 34, wherein said assay is an *in vitro* assay.

38. (Withdrawn) A Chfr inhibitor identified by the method of claim 34.

39. (Withdrawn) A method of retarding the growth of a cancer cell, said method comprising administering to said cell a Chfr inhibitor that enhances the sensitivity of said cell to mitotic stress.

40. (Withdrawn) The method according to claim 39 further comprising administering to said cancer cell an agent which disrupts microtubule function.



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41. (Withdrawn) The method according to claim 39, wherein said method kills said cancer cell.

42. (Withdrawn) A method of assessing the sensitivity of a tumor cell to an agent which disrupts microtubule function, said method comprising examining said cell for a characteristic selected from the group consisting of:

(a) the substantial absence of a *chfr* gene;

(b) the substantial absence of Chfr protein;

(c) the substantial absence of Chfr-mediated ubiquitin-protein ligase activity; and

(d) a mutation in the *chfr* gene;

wherein the identification of any of said characteristics provides an indication that said tumor cell is sensitive to an agent which disrupts microtubule function.



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